

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (Currently amended) A method for administering a photodynamic therapy to destroy or impair target cells expressing a VEGF receptor in a mammalian subject, comprising the steps of:

(a) administering to the subject a therapeutically effective amount of a targeted photosensitizer compound having a characteristic light absorption waveband, wherein:

the said targeted photosensitizer compound selectively binds
binding with the target cells, but does not bind binding with non-target
cells, and

the said photosensitizer compound being inert upon administration
is targeted to a VEGF receptor;

(b) transcutaneously irradiating at least a portion of the mammalian subject in which the target cells to which the targeted photosensitizer compound has bound are is disposed, with light having a waveband corresponding at least in part to the characteristic light absorption waveband of the said targeted photosensitizer compound; compound, wherein and

(c) ~~ensuring that an intensity of the light used for the step of~~
~~transcutaneously irradiating is substantially less than 500 mw/cm², and that a~~
~~total fluence of the light used for irradiating is sufficiently high to activate said~~
~~targeted photosensitizer compound, said light activating the targeted~~
~~photosensitizer compound, causing said target cells to be destroyed or impaired.~~

the intensity of the light used for the step of irradiating and the
duration of irradiation are selected such that the target cells are destroyed and
the non-target tissue through which the light passes remains undamaged.

2. (Original) The method of claim 1, further comprising the step of allowing sufficient time for any targeted photosensitizer compound that is not

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bound to the target cells to clear from the non-target cells of the mammalian subject prior to the step of irradiating.

3. (Currently amended) The method of claim 1, wherein the target cells are comprised in a target tissue selected from the group consisting of [[:]] a vascular endothelial tissue, an abnormal vascular wall of a tumor, a solid tumor, a tumor of head, a tumor of a neck, a tumor of a gastrointestinal tract, a tumor of a liver, a tumor of a breast, a tumor of a prostate, a tumor of a lung, a nonsolid tumor, malignant cells of one of a hematopoietic tissue and a lymphoid tissue, lesions in a vascular system, a diseased bone marrow, and diseased cells in which the disease is one of an autoimmune and an inflammatory disease.

4. (Original) The method of claim 3, wherein the target tissue is a lesion of a type selected from the group consisting of atherosclerotic lesions, arteriovenous malformations, aneurysms, and venous lesions.

5. (Original) The method of claim 1, wherein the step of irradiating comprises the step of providing a light source that is disposed internal to an intact skin layer of the mammalian subject and wherein said light source is activated to produce the light.

6. (Currently amended) The method of ~~claim 5~~ claim 1, wherein the step of irradiating comprises providing a light source that is disposed external to an intact skin layer of the mammalian subject and wherein the said light source is activated to produce the light.

7. (Currently amended) The method of claim 1, wherein the photosensitizer compound comprises one of:

- (a) a targeted photosensitizing agent;
- (b) a photosensitizing agent delivery system that delivers the targeted photosensitizing agent to bind with the target cells; and
- (c) a prodrug that produces a prodrug product, the said prodrug product selectively binding to the target cells.

8. (Currently amended) The method of claim 7, wherein the said photosensitizing agent is conjugated to a ligand that specifically binds to the

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VEGF receptor of target cells; wherein the ligand ~~and that~~ is selected from the group consisting of ~~[[:]]~~ an antibody ~~[[,]]~~ or bindable fragment thereof; a peptide; a polymer; a glycoprotein; and a lipoprotein.

9. (Currently amended) The method of claim 7, wherein the said photosensitizer compound is selected from the group consisting of indocyanine, methylene blue, toluidine blue, aminolevulinic acid, chlorins, phthalocyanines, porphyrins, purpurins, bacteriochlorins, merocyanines, psoralens and texaphyrins.

10. (Original) The method of claim 1, wherein the step of irradiating is carried out for a time interval of from about 4 minutes to about 72 hours.

11. (Original) The method of claim 1, wherein the step of irradiating is carried out for a time interval of from about 60 minutes to about 48 hours.

12. (Original) The method of claim 1, wherein the step of irradiating is carried out for a time interval of from about 2 hours to about 24 hours.

13. (Original) The method of claim 1, wherein the total fluence of the light used for irradiating is between about 30 Joules and about 25,000 Joules.

14. (Original) The method of claim 1, wherein the total fluence of the light used for irradiating is between about 100 Joules and about 20,000 Joules.

15. (Original) The method of claim 1, wherein the total fluence of the light used for irradiating is between about 500 Joules and about 10,000 Joules.

16. (Currently amended) A method for administering a photodynamic therapy to a ~~transeutaneously and selectively destroying or impairing~~ target tissue in a mammalian subject, comprising ~~the step of:~~

(a) administering to the mammalian subject a therapeutically effective amount of a first conjugate comprising a first member of a ligand-receptor binding pair conjugated to an antibody or an antibody fragment, wherein the said antibody or the said antibody fragment selectively binds to an antigen of a VEGF receptor on the target tissue, ~~said first conjugate being inert upon administration;~~

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(b) administering to the mammalian subject a therapeutically effective amount of a second conjugate comprising a second member of the ligand-receptor binding pair, conjugated to a photosensitizer compound, ~~said second conjugate being inert upon administration~~; and

(c) irradiating at least a portion of the mammalian subject in which the target tissue that is bound to the ~~said~~ antibody or the ~~said~~ antibody fragment is disposed, using light having a waveband corresponding at least in part to the characteristic light absorption waveband of the ~~said~~ photosensitizer compound, thereby activating the ~~said~~ photosensitizer compound and destroying or impairing the ~~said~~ target tissue.

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17. (Currently amended) The method of claim 16, wherein the ligand-receptor binding pair is selected from the group consisting of [[:]] biotin-streptavidin, chemokine-chemokine receptor, growth factor-growth factor receptor, and antigen-antibody.

18. (Currently amended) A method for transcutaneously destroying or impairing a target tissue in a mammalian subject, comprising the steps of:

(a) administering to the subject a therapeutically effective amount of an ~~energy activated delivery system, wherein said system comprises an energy-activated energy-activated agent that absorbs energy and destroys a target tissue to which it is bound, wherein the energy-activated agent is which is inert upon administration; and a ligand conjugated to a ligand said energy activated agent, said ligand binding to a that binds to a VEGF receptor on the target tissue with specificity, so that binding of the ligand to a non-target tissue is minimized;~~

(b) irradiating at least a portion of the subject with energy at a wavelength that activates ~~said~~ the energy-activated ~~energy-activated~~ agent, whereupon ~~said activated~~ the targeted tissue is destroyed or impaired ~~thereby,~~ wherein

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the intensity of the energy used for the step of irradiating and the duration of irradiation are selected such that the target cells are destroyed and the non-target tissue through which the energy passes remains undamaged.

19. (Canceled)

19 20. (Currently amended) The method of claim 18, wherein the target tissue is selected from the group consisting of [[:]] a vascular endothelial tissue; and abnormal vascular wall of a tumor; a solid tumor in one of the head, the neck, the gastrointestinal tract, the liver, the breast, the prostate, and the lung; a nonsolid tumor; malignant cells in hematopoietic tissue; malignant cells in lymphoid tissue; lesions in a vascular system; diseased bone marrow; cells afflicted by an autoimmune; and cells afflicted with an inflammatory disease.

19 21. (Currently amended) The method of claim 18, wherein the said energy is ultrasound energy.

22. Claims 22 - 30 (Canceled)

23 31. (New) A method to occlude a blood vessel in a mammalian subject, comprising:

- (a) administering to the subject a targeted photosensitizer compound;
- (b) transcutaneously irradiating at least a portion of the mammalian subject with light of a wavelength and total fluence sufficient to activate the photosensitizer compound at a time when circulating targeted photosensitizer compound is high, wherein the compound is activated within the lumen of the blood vessel, wherein:

a combination of an intensity of light and a duration of light is selected for irradiating such that non-target tissue through which the light passes remains undamaged yet the targeted photosensitizer compound is activated, whereby the blood vessel is occluded.

23 32. (New) The method of claim 31, wherein the activated targeted photosensitizer causes damage to targeted endothelium.

23 33. (New) The method of claim 31, wherein the activated targeted photosensitizer causes platelet activation.

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²⁴34. (New) The method of claim ²¹31, wherein the activated targeted photosensitizer causes injury to circulating blood elements.

²⁵35. (New) The method of claim ²⁴34, wherein the circulating blood elements are red blood cells.

²⁶36. (New) The method of claim ²¹31, wherein the targeted photosensitizer crosses fenestrations in tumor vessels.

²⁷37. (New) The method of claim ²¹31, wherein the targeted photosensitizer binds to an abluminal side of the blood vessel.

²⁸38. (New) The method of claim ²¹31, wherein the targeted photosensitizer binds to a luminal side of the blood vessel.

²⁹39. (New) The method of claim ²¹31, wherein the duration of light used for irradiating is further selected to prevent blood vessel recanalization.

³⁰40. (New) The method of claim ²¹31, wherein the targeted photosensitizer binds to a specific endothelial receptor.

³¹41. (New) The method of claim ³⁰40, wherein the receptor is a VEGF receptor.